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10/531,526	02/08/2006	Robert E Dudley	05046509	9100

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EXAMINER	
HOUGHTLING, RICHARD A	
ART UNIT	**PAPER NUMBER**
1617	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,526	DUDLEY, ROBERT E	
	Examiner	Art Unit	
	RICHARD A. HOUGHTLING	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-48 are pending and examined on their merits, herein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

2. Claims 1-13, 15-34 and 36-48 are rejected under 35 U.S.C. 102(e) as being anticipated by van der Hoop (U.S. PG Publication 2003/0027804).

Van der Hoop teaches methods and compositions for treatment of hormone deficiencies including hypogonadism (see pp. 2-3, ¶ [0015-0019]; p. 7 ¶ [0071]) and erectile dysfunction (see p. 7, ¶ [0071]) involving administration of 1) a sex hormone binding globulin inhibitor, 2) a steroid (such as testosterone), and 3) other pharmaceutical agents for improving sexual performance or impotence, treating erectile dysfunction and increasing libido (see Abstract; p. 8, ¶ [0072], lines 35-42) such as the phosphodiesterase inhibitor—sildenafil citrate or another pharmaceutical agent administered after the steroid treatment, such as yohimbine or papaverine (p. 12, ¶ [0109]). Van der Hoop further teaches a pharmaceutical composition for administration to the skin, a hydroalcoholic gel formulation of testosterone, a penetration enhancer, a C1-C4 alcohol and a gelling agent (see p. 10, ¶ [0091] and Table 6). Many penetration enhancers are taught by Van der Hoop, including isopropyl myristate which is a C17 fatty acid which may be present in the formulation at about 0.5% w/w as calculated from the values found in Table 6 (p. 10). Possible alcohols which may be included in the gel formulation are ethanol, 2-propanol (isopropanol) or n-propanol (see p. 9, ¶ [0082]). Thickeners such as polyacrylic acid (i.e., CARBOPOL®) and carboxymethylcellulose are found p. 9 ¶ [0080]. Example 4 (p. 15, ¶ [0134-0135] shows that the hydroalcoholic gel may be administered as either 5.0 g/day Androgel® or as 10.0 g/day Androgel®, thus as single or a divided dose; the sildenafil citrate (50 mg) tablet was to be administered 1 hr before intercourse after at least 1 day of methyltestosterone and Androgel® therapy; and preferably the Androgel® is administered for a sufficient number of days to achieve steady state levels of testosterone, especially in hypogonadal men (see p. 13, ¶ [0115]).

In addition to the hydroalcoholic testosterone gel (i.e., Androgel®), Van der Hoop teaches that additional pharmacological agents may be administered to treat erectile dysfunction. As mentioned above, a phosphodiesterase inhibitor, which acts on type III, type IV or type V enzymes (see p. 11, ¶ [0105-0108]). When sildenafil is utilized, a dose of 50 mg is orally administered (see p. 15, Example 4 ¶ [0134]). Constituents of the composition (100 g) may also be varied containing about 0.1 to about 10 g of testosterone, about 0.1 to about 5.0 g isopropyl myristate, about 0.1 to about 5.0 g of CARBOPOL®, and about 30 to 98 g ethanol (see p. 10, ¶ [0092]). Active agents of the invention may be administered in the form of salts, including the use of sodium hydroxide (see p. 13, ¶ [0116]). Van der Hoop further claim a kit comprising an orally deliverable methyltestosterone, a steroid such as testosterone, which further comprises a pharmaceutical agent for treatment of erectile dysfunction, such as sildenafil citrate or papaverine or apomorphine (see claims 30, 33-37 and 40-44). Van der Hoop teaches each and every element of instant claims 1-13, 15-34 and 36-48.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 14 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van der Hoop as applied to claims 1-13, 15-34 and 36-48 above, and further in view of Hussain et al. (see PTO-892, U.S. Patent 6,200,591).

Van der Hoop is relied upon for the reasons stated above.

Van der Hoop does not teach the limitation of administration of sildenafil citrate by an intranasal route in an amount of about 10 mg, 20 mg or 40 mg (instant claim 14).

Van der Hoop does not teach the limitation of oral administration of apomorphine in an amount of about 2 mg to about 3 mg (instant claim 35).

Hussain et al. teaches a method of intranasal administration of sildenafil citrate to treat erectile dysfunction (see abstract, Figure 1; col. 2, lines 58-64; col. 10, Examples 2 or 3), which may additionally include other pharmaceutical agents such as, apomorphine, papaverine, phentolamine and phenoxybenzamine (see col. 3, lines 23-28; col. 10, Examples 4 or 5). Administration of one spray into each nostril will deliver a total of 30 mg of sildenafil hydrochloride and 1 mg of apomorphine hydrochloride (see col. 10, Example 4, lines 52-54). Hussain et al. also teaches that combination therapies that use sildenafil and apomorphine or other pharmaceutical agents (papaverine, phentolamine or phenoxybenzamine) may be administered simultaneously or sequentially in separate formulations to reach a combined effect; which the amounts and regime of administration is adjusted by the practitioner initially at lower doses and titrating up until desired effect is reached (see col. 3, lines 26-28; col. 8 lines 3-12).

At the time of Applicant's invention, one of ordinary skill in the art would have found it *prima facie* obvious to substitute the intranasal formulation of sildenafil taught by Hussain et al. into the method for treatment of erectile dysfunction found in subjects suffering from hypogonadism as taught by Van der Hoop. The motivation to do so is found in Hussain et al. which teaches that intranasal administration of sildenafil permits a rapid onset of effect at a

reduced dose required to produce a beneficial effect (see col. 2, lines 65-67 to col. 3 lines 1-2) and further that a practitioner will use titration regimens to optimize the dosing amounts needed especially for combination therapy with additional pharmaceutical agents such as apomorphine.

Conclusion

1. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard A. Houghtling whose telephone number is (571) 272-9334. The examiner may normally be reached Mon-Thurs 8:30 am - 5:00 pm and alternate Fridays 8:30 am - 12:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan may be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571- 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RAH
Patent Examiner

/San-ming Hui/

Primary Examiner, Art Unit 1617